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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,881	09/11/2003	Harlan W. Waksal	11245/46403	8515

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
10/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,881	WAKSAL ET AL	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 31-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 31-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/26/2007 has been entered.

2. The amendment filed 7/26/2007 is acknowledged.

Claims 1, 3, 24 and 31-48 are pending and examined on the merits.

Claim Rejections Withdrawn:

3. The rejection of claims 1, 3, 24, 31-48 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment to the claims.

Claim Rejections Maintained and New Grounds of Rejection:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 1, 3, 24, 31, 32, 34, 38, and 45 rejected under 35 U.S.C. 102(a) as being anticipated by Ezekiel (Proceedings of ASCO, 17: Abstract No. 1522, 1998, April 15; cited in IDS).

Ezekiel teaches administration of Mab C225 in combination with radiation treatment to patients with squamous cell carcinoma of the head and neck (SCCHN), where the administration of Mab C225 occurs before the radiation treatment and also during the radiation treatment. Therefore, Ezekiel teaches a method that is the same as that claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 3, 24, 31-39, 41, 43, 45 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bos (ASCO Annual Meeting, Abstract No. 1381, 1996) in view of Saleh (Saleh, M. et al., Proceedings of the American association for Cancer Research, 37: 612, Abstract #4197, 1996, March; cited in the IDS).

Bos teaches a method of treating patients with diverse tumor types (head and neck, prostate, lung, esophagus, pancreas and kidney) with an anti-EGFR antibody, the C225 antibody. Bos reports that treatment with the C225 antibody resulted in minor responses and patients having no disease progression. Bos fails to teach administration of the C225 antibody in combination with radiation therapy.

However, Saleh teaches that in a mouse xenograft model, the combination of radiation and an anti-EGFR antibody resulted in better tumor control. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have combined the C225 antibody of Bos with radiation therapy for the purpose of inhibit the growth of tumors in human patients. One would have been motivated by the teachings of Saleh that the combination of an anti-EGFR antibody and radiation therapy resulted in greater efficacy of treatment of the tumors.

Claims 31-39 include limitations concerning the order in which the antibodies and radiation are administered. The combination of Saleh and Goldstein does not explicitly teach each and every administration schedule of claims 31-39. However, it would be obvious to one of ordinary skill in the art of treating cancer patients how to optimize a treatment schedule. Such optimization of treatment does not appear to add an inventive step to the claimed inventions. See **MPEP 2144.05**: A. Optimization Within Prior Art Conditions or Through Routine Experimentation

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons,

there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

6. Claims 1, 3, 24, 31-41, 43-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bos (ASCO Annual Meeting, Abstract No. 1381, 1996) in view of Saleh (Saleh, M. et al., Proceedings of the American association for Cancer Research, 37: 612, Abstract #4197, 1996, March; cited in the IDS), and further in view of Goldstein (Goldstein, N.I. et al, Clinical Cancer Research, 1: 1311-1318, 1995; cited in a previous Office action).

The claims include methods of treatment of breast, bladder or ovarian cancer. The combination of Bos and Saleh does not teach treatment of either breast, bladder or ovarian cancer. However, Goldstein teaches that EGFR is expressed on many tumor types including breast, ovarian, bladder, head and neck, and prostatic carcinoma. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the methods of Bos and Saleh to treat breast, ovarian or bladder cancer that also expressed EGFR, because Bos teaches that an anti-EGFR antibodies are useful in a diverse array of human cancer patients with various types of cancer, and because Goldstein teaches that EGFR is expressed on many tumor types.

7. Claims 1, 3, 24, 31-39, 41-43, 45, 47 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bos (ASCO Annual Meeting, Abstract No. 1381, 1996) in view of Saleh (Saleh, M. et al., Proceedings of the American association for Cancer Research, 37: 612, Abstract #4197, 1996, March; cited in the IDS), and further in view of Arnold (U.S. 5,736,534; issued April 7, 1998; effective filing date July, 29, 1996; cited in the IDS).

The claims include methods of treatment of colon cancer or brain cancer. The combination of Bos and Saleh does not teach treatment of colon cancer. However, Arnold teaches methods of treatment of cancers such as renal, liver, kidney, bladder, breast, gastric, ovarian, colorectal, prostate, pancreatic, lung, vulval, thyroid, hepatic carcinomas, sarcomas, glioblastomas, and various head and neck tumors comprising an EGFR targeted therapy (quinzolines) in combination with radiation (see col. 20, lines 24). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the methods of Bos and Saleh to treat colon cancer that also expressed EGFR, because Bos teaches that an anti-EGFR antibodies are useful in a diverse array of human cancer patients with various types of cancer, and because Arnold teaches that EGFR is expressed on colorectal cancers and that anti-EGFR treatment methods in combination with radiation therapy are useful for the treatment of colorectal cancer.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1,3, 24 and 31-48 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 11/206,825. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of copending 11/206,825 anticipate the claims of the instant case. The claims of the copending application are drawn to methods of inhibiting tumor growth comprising administering antibodies that bind to EGFR, at least one chemotherapeutic agent and radiation therapy. Thus, these claims are a species of the claims of the instant application.

Applicant argues that this rejection should be withdrawn because application 11/206,825 is not co-owned with the instant application and does not have the same inventorship as Applicant's instant application, and that there is only one inventor in common between the two applications. This is not found persuasive because a double patenting rejection is made when there is at least one common inventor *or* a common assignee. Therefore the rejection is maintained for the reasons of record.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
October 1, 2007

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER